

## REMARKS

## I. Amendments to the Specification

The Abstract has been amended to remove the subject matter of withdrawn claims 10 and 11 and thus incorporate only subject matter of the claims, as currently-amended. No new matter has been added by way of this amendment.

## II. Claim Amendments & Status of the Claims

Claims 1-9 have been amended. Support for the material in amended claims 1-9 can be found throughout the present specification, including for example at Figure 2, and at ¶¶ 0020, 0031, 0041, 0067, and 0078. Support for the material in added claims 12 and 13 can be found in the specification at p.7, Example 2, and p. 3, ¶ 0023 respectively. By this amendment, no new matter has been added to this application.

Claims 1-11 are currently pending. Claims 10 and 11 were withdrawn according to the response to restriction requirement filed September 8, 2005. Claims 12 and 13 have been added by way of this amendment.

### III. Rejections under 35 U.S.C. § 103(a)

Claims 1-9 stand rejected under 35 U.S.C. § 103(a) as obvious over Igarashi et al., Biosci., Biotech., Biochem., (“Igarashi”), and Yamahara, J., JP2002187845 (abstract) (“Yamahara”). The Examiner contends that Igarashi teaches the administration of dihydroquercetin to reduce total body fat and mass, and refers to the data in Table 1 (p.514) highlighting a decrease in total liver cholesterol. Additionally, the Examiner contends that Yamahara teaches the use of saccharides from the buds of *Aralia elata* plant as an anti-obesity drug. The Examiner states that in view of these teachings, one skilled in the art would have been motivated to combine dihydroquercetin (i.e. taxifolin) with an araloside to treat obesity.

For a claim to be obvious under 35 U.S.C. § 103(a), three criteria must be satisfied:

- (i) there must be some suggestion or motivation to combine or modify the cited references,
- (ii) there must be a reasonable expectation of success of combining or modifying the cited references, and
- (iii) the combined references must teach each and every limitation of the claimed invention.

*Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000). Applicants respectfully submit that these criteria have not been met, and thus traverse this rejection and request reconsideration.

First, Applicants disagree with the Examiner's interpretation of Igarashi and the data referred to therein. Specifically, the Examiner used the data in Table I (Igarashi, p. 514) to support an argument that taxifolin helps reduce weight. However, a close examination of the data in Table I, and accompanying text, reveals that taxifolin administration actually had no statistically significant effect on food intake or on body weight gain (*see* data, Table I). In fact, the cited reference states: "As shown in Table I, the ingestion of astilbin and [or] taxifolin *did not statistically affect* the daily food intake, *body weight gain*, or the concentrations of serum total cholesterol, HDL-cholesterol, triacylglycerol, and phospholipid..." (emphasis added). Igarashi teaches that while taxifolin may reduce total liver cholesterol, it is ineffective alone at reducing weight. The instant invention is not directed to reducing total liver cholesterol, and Igarashi teaches no significant impact on body weight gain. Notably, the data shown in column 4 of Table I indicate that rats fed casein + taxifolin ("20C + T") actually *gained*  $36 \pm 2$  grams of weight in 10 days. To that extent, Igarashi teaches away from the use of taxifolin as an obesity treatment. Therefore, the findings taught by Igarashi would certainly not suggest or motivate one skilled in the art to use taxifolin as a regimen for reducing weight, as asserted by the Examiner. Nor would the data provided by Igarashi provide a reasonable expectation of success in using taxifolin as a weight reducing treatment alone, much less provide an obvious improvement in conjunction with another agent.

Second, although Yamahara teaches use of saccharides from *Aralia elata* as an anti-obesity drug, reliance on Yamahara in combination with Igarashi is misplaced. As noted above, the combined

references must teach each and every limitation of the claimed invention, and there must be some suggestion or motivation to combine or modify the cited references. By combining Igarashi and Yamahara, one skilled in the art would not have arrived at the presently claimed invention because, as noted above, Igarashi does not disclose or suggest that taxifolin is an effective obesity treatment. Thus, there would be no motivation to use taxifolin/araloside dual therapy to treat obesity because Igarashi alone does not teach that taxifolin has a weight-reducing effect.

Finally, the claims have been amended to call for aralosides A, B, C, and D derived from *Aralia* root bark. In contrast, the cited art refers to aralosides present in *Aralia* buds. The declaration of Zakir Ramazanov (which accompanies this response) reports on a comparison of aralosides obtained from *Aralia* root bark and *Aralia* bud. In the declaration, it is first noted that the aralosides obtained from *Aralia* bud are structurally different from the root bark-derived aralosides (see Ramazanov, ¶ 8). Specifically, HPLC analysis revealed that *Aralia* root bark-derived aralosides include aralosides A, B, C, and D, which are now included as claim limitations, while *Aralia* buds do not contain aralosides A, B, C, and D. Furthermore, the declaration describes experimental data from a 15-week study wherein subjects were treated with *Aralia* root bark or bud extracts. A weight reducing effect was observed only in those individuals that received the *Aralia* root bark extract (see Ramazanov, ¶¶ 11, 12). Finally, the Ramazanov declaration reports that aralosides, (A, B, C, and D), obtained from *Aralia* root bark (and not *Aralia* bud), have an effect on adipocyte perilipin content and synthesis, the underlying mechanism of weight control (see Ramazanov, ¶¶ 13, 14). It is clear that the *Aralia* root bark extract in combination with *E. chrysolepis* extract, containing, *inter alia*, dihydroquercetins, promotes loss of both body weight and body fat, while *Aralia* root bark extract in combination with *E. chrysolepis* extract has little or no effect.

The collective results of the HPLC experiments and 15-week study described in the Declaration establish that:

- a) *Aralia* root bark and buds contain different triterpene saponins, and these saponins have disparate pharmacological activities;
- b) *Aralia* root bark extract, in combination with *E. chrysolepis* extract, containing, *inter alia*, dihydroquercetins, promotes loss of both body weight and body fat in obese, non-diabetic women;

- c) adipocyte perilipin content was significantly reduced in adipocytes from patients treated with *Aralia* root bark + dihydroquercetin, but not *Aralia* bud extract + dihydroquercetin; and
- d) adipocytes from the patients treated with *Aralia* root bark + dihydroquercetin synthesized significantly less perilipin protein than did patients treated with *Aralia* bud extract + dihydroquercetin.

These are believed to be unexpected results. Those skilled in the art would not have expected a difference in the weight-reducing effects of *Aralia* root bark and *Aralia* bud extracts.

It is respectfully submitted that the present claims are not obvious in view of the cited references. Igarashi does not teach that taxifolins reduce weight, and thus there is neither a motivation to combine Igarashi with Yamahara, nor a reasonable expectation of success upon making such a combination. Moreover, the present amendment limits the invention to aralosides A, B ,C, and D obtained from *Aralia* root bark, which is demonstrably outside the teachings of Yamahara and fully supported in the specification. Thus, in light of the amendment, comments, and the Ramazanov declaration, withdrawal of the rejection is believed to be in order.

Based on the preceding comments and amendments, the present claims are believed to be in condition for allowance and such action is earnestly solicited.

Dated:

Respectfully submitted,

By \_\_\_\_\_

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